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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/871,610	06/01/2001	Glenn McGall	2719.2016-001	1735

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EXAMINER	
FORMAN, BETTY J	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 08/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/871,610	MCGALL ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 January 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

FINAL ACTION

1. This action is in response to papers filed 3 January 2003 in which claims 1-15 were amended. All of the amendments have been thoroughly reviewed and entered. The previous rejections in the Office Action dated 3 October 2002 are withdrawn in view of the amendments. All of the arguments have been thoroughly reviewed but are deemed moot in view of the amendments, withdrawn rejections and new grounds for rejection. New grounds for rejection, necessitated by amendment are discussed.

Claims 1-15 are under prosecution.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 1-6 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gamble et al (U.S. Patent No. 5,981,733, issued 9 November 1999).

Regarding Claim 1, Gamble et al disclose a method of preparing a nucleic acid array on a support wherein each nucleic acid occupies a separate known region of the support said synthesis comprising: activating a region of the support, attaching a nucleotide to a first

region, said nucleotide having a masked reactive site linked to a protective group, repeating steps of activating and attaching on other regions of the support whereby each of said other regions has bound thereto another nucleotide comprising a masked reactive site wherein said another nucleotide may be the same of different from that used in the first step, removing the protecting group from one of the nucleotides bound to one of the regions of the support to provided a region bearing a nucleotide having an unmasked reactive site, binding an additional nucleotide to the nucleotide with an unmasked reactive site, and repeating the steps of removing and binding until a desired plurality of nucleic acids is synthesized, each occupying a separate known region wherein the surface of the substrate is maintained in a position which is vertical or about 30 degrees of vertical and wherein the substrate is rotated around an axis perpendicular to said surface by an amount of from about 20 degrees to about 180 degrees, said rotating being done prior to and subsequent to at least one of said attaching and binding steps (Column 12, line 18-Column13, line 54 and Claims 9 & 10) whereby said rotated support has a different position relative to the support in the prior attaching step (i.e. moved along the X-Y axis, Column 12, lines 52-54) and wherein at least one of said attaching or binding steps occurs after the support is rotated i.e. during synthesis, the support is cyclically moved between the jetting system and the reaction chamber, Column 5, lines 66-67). Gamble et al further teach the method wherein the support is held in a vertical position for reagent delivery (Column 4, lines 21-34) whereby the entire surface of the substrate is coated with the reagent and wherein the reagents include any reagents necessary for synthesis (Column 4, lines 40-46) whereby the substrate is in a vertical position during activation step (a) and clearly suggests that the substrate may be in a vertical position during attachment step (b). Furthermore, Gamble et al clearly provide motivation to position the substrate in vertical position during the attachment step when they teach that a vertical position provides complete coverage of the activated area and eliminates bubbles in the reagent solution (Column 4, lines 21-34). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was

made to vertically position the substrate of Gamble et al during the attachment step to thereby insure complete coverage of the activated area and to eliminate problematic bubbles as they desire (Column 4, lines 21-34).

Regarding Claims 2 & 3, Gamble et al disclose the method wherein said rotating is conducted prior to or subsequent to at least 50% (Claim 2) and at least 80% (Claim 3) of said attaching and binding (Column 12, line 18-Column19, line 54 and Claim 9).

Regarding Claims 4 & 5, Gamble et al disclose the method wherein said rotating in an amount of from about 70 to about 105 degrees (Claim 4) and of about 90 degrees (Claim 5) (Column 12, line 18-Column19, line 54 and Fig. 12).

Regarding Claim 6, Gamble et al disclose the method wherein the interface is vertical (i.e. the support is vertical) and said rotating is an amount of about 90 degrees (Column 12, line 18-Column19, line 54; Claims 9 & 10; and Fig. 12).

Regarding Claim 14, Gamble et al disclose the method wherein each different nucleic acid is in a region having an area of less than about 1 cm^2 (Column 10, lines 12-15 and Column 12, lines 21-24).

4. Claims 7 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gamble et al (U.S. Patent No. 5,981,733, issued 9 November 1999) in view of Bass et al (U.S. Patent No. 6,440,669 B1, filed 10 November 1999).

Regarding Claim 7, Gamble et al teach a method of preparing a nucleic acid array on a support wherein each nucleic acid occupies a separate known region of the support said synthesis comprising: activating a region of the support, attaching a nucleotide to a first

region, repeating steps of activating and attaching on other regions of the support, removing the protecting group from one of the nucleotides bound to one of the regions of the support, binding an additional nucleotide to the nucleotide with an unmasked reactive site, and repeating the steps of removing and binding until a desired plurality of nucleic acids is synthesized, wherein the substrate is rotated around an axis perpendicular to said surface by an amount of from about 20 degrees to about 180 degrees, said rotating being done prior to and subsequent to at least one of said attaching and binding steps and wherein the substrate is square and a surface of the substrate (i.e. interface) is maintained in a position which is vertical or about 10 degrees of vertical (Column 12, line 18-Column19, line 54 and Claims 9 & 10) but they do not teach the substrate is substantially square silica chip. However, square planar silica substrates were well known in the art at the time the claimed invention was made as taught by Bass et al (Column 5, lines 38-67) who teach a similar method of preparing a nucleic acid array comprising: activating a region of the support, attaching a nucleotide to a first region, repeating steps of activating and attaching on other regions of the support, removing the protecting group from one of the nucleotides bound to one of the regions of the support, binding an additional nucleotide to the nucleotide with an unmasked reactive site, and repeating the steps of removing and binding until a desired plurality of nucleic acids is synthesized (Column 11, lines 24-64). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the square planar silica substrate of Bass et al to the substrate of Gamble et al based on it's well known use as an array substrate and therefore known success as an array substrate for the obvious benefits of obtaining expected results.

Regarding Claim 8, Gamble et al teach the method wherein the it is preferable that the substrate be positioned so that the maximal surface area of the substrate is covered by fluid rising from the bottom inlet port (Column 4, lines 21-34) but they do not teach the substrate held with one of the four vertices pointing downward. However, it would have been obvious to

one of ordinary skill in the art at the time the claimed invention was made to modify the position of their substrate such that one of the vertices is pointing downward thereby maximizing the surface area covered by fluid rising across the surface for the obvious benefits of coving the entire surface of the substrate as they desire (Column 4, lines 30-34).

5. Claims 9-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gamble et al (U.S. Patent No. 5,981,733, issued 9 November 1999) in view of Brennan (U.S. Patent No. 5,985,551, issued 16 November 1999).

Regarding Claims 9-13, Gamble et al teach a method of preparing a nucleic acid array on a support wherein each nucleic acid occupies a separate known region of the support said synthesis comprising: activating a region of the support, attaching a nucleotide to a first region, repeating steps of activating and attaching on other regions of the support, removing the protecting group from one of the nucleotides bound to one of the regions of the support, binding an additional nucleotide to the nucleotide with an unmasked reactive site, and repeating the steps of removing and binding until a desired plurality of nucleic acids is synthesized, wherein the surface of the substrate is maintained in a position which is vertical or about 30 degrees of vertical and wherein the substrate is rotated around an axis perpendicular to said surface by an amount of from about 20 degrees to about 180 degrees, said rotating being done prior to and subsequent to at least one of said attaching and binding steps (Column 12, line 18-Column19, line 54 and Claims 9 & 10) and wherein each nucleic acid region have center-to-center spacing of 50 microns to 2 millimeters (Column 10, lines 12-

15 and Column 12, lines 21-24) but they do not specifically teach the substrate comprises at least 10 different nucleic acids (Claim 9); at least 100 different nucleic acids (Claim 10); at least 1,000 different nucleic acids (Claim 11); at least 10,000 different nucleic acids (Claim 12); at least 100,000 different nucleic acids (Claim 13). However, high density arrays were well known in the art at the time the claimed invention was made as taught by Brennan who teach that there is a need for high density arrays which can be produced rapidly and conveniently (Column 2, lines 1-7). Specifically, Brennan teaches a similar method of preparing a nucleic acid array having regions of 50 microns to 2 millimeters comprising: activating a region of the support, attaching a nucleotide to a first region, repeating steps of activating and attaching on other regions of the support, removing the protecting group from one of the nucleotides bound to one of the regions of the support, binding an additional nucleotide to the nucleotide with an unmasked reactive site, and repeating the steps of removing and binding until a desired plurality of nucleic acids is synthesized wherein the array comprising at least 100,000 regions of 50 microns to 2 millimeters (Column 2, lines 17-19 and Example 2, Column 7, line 36-Column 8, line 10). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the high density array teaching of Brennan to the array of Gamble et al and to form at least 10; at least 100; at least 1,000; at least 1,000, at least 100,000 different nucleic acids on the surface based on the teaching of Brennan wherein methods for producing high density arrays rapidly, conveniently and accurately is needed and desired (Column 2, lines 1-7). Therefore, it would have been obvious to one skilled in the art to modify method of making arrays of Gamble et al by producing high density arrays for the expected benefits of speed, convenience and accuracy as taught by Brennan (Column 2, lines 1-7).

Response to Arguments

6. Applicant argues that Gamble et al do not teach that the substrate is rotated such that the substrate has a different position relative to the support in the prior attaching or binding step. The argument has been considered but is not found persuasive because, as noted above, Gamble et al specifically teach the substrate is cyclically rotated between synthesis steps (Column 5, lines 66-67) and movement of the substrate along the X-Y axis between attaching steps to deliver reagents to individual loci (Column 12, lines 52-58) whereby the substrate is in a position different from the prior attaching step. Therefore, Gamble et al teach the substrate is rotated and at a position different from that of the prior attachment step as claimed.

Applicant further argues that Bass et al and Brennan do not remedy the deficiencies of Gamble et al because they do not teach the substrate is rotated such that the substrate has a different position relative to the support in the prior attaching or binding

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:30 TO 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
Primary Examiner
Art Unit: 1634
August 25, 2003